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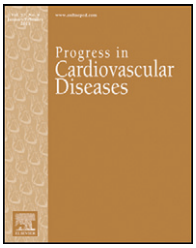

Medical Management of Asymptomatic Carotid Artery Stenosis

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ABSTRACT

Carotid artery atherosclerosis is a major risk factor for both stroke and cardiovascular disease. Appropriate management of asymptomatic patients with carotid artery stenosis (CAS) remains unclear. Although several randomized clinical trials support revascularization in asymptomatic patients with severe CAS to reduce stroke risk, the participants in these trials did not receive optimal medical therapy (OMT) by today's standards. For many individuals, medical therapy may provide excellent risk reduction without the periprocedural risk of endarterectomy or stenting. In this review, we discuss the risk factors for CAS and stroke and examine the data for each component of OMT in these patients.

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Statement of Conflict of Interest: see page XX.

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Abbreviations and Acronyms

ACAS = Asymptomatic Carotid Artery Stenosis

ACST = Asymptomatic Carotid Surgery Trial

ACT = Asymptomatic Carotid Stenosis Trial

BMI = Body mass index

BP = Blood pressure

CAS = Carotid artery stenosis

CEA = Carotid endartarectomy

CREST = Carotid Revascularization for Primary Prevention of Stroke

CVD = Cardiovascular disease

DM = Diabetes mellitus

HTN = Hypertension

ICA = Internal carotid artery

LDL-C = Low-density lipoprotein cholesterol

MI = Myocardial infarction

OMT = Optimal medical therapy

TIA = Transient ischemic attack

US = United States

Background

Asymptomatic carotid artery stenosis (CAS) is a common form of atherosclerotic vascular disease with a prevalence that increases with age. Internal carotid artery (ICA) stenosis of at least 50% will develop in up to 3–4% of the general population in the United States (US).[1] The disease begins to develop as early as age 40. The prevalence steadily increases to as high as 11% in men age 80 or greater.[2,3] Men are more likely to be affected than women, and certain racial subgroups, including Caucasians and Native Americans, are at highest risk.[1,3] Although atherosclerosis is the most common cause of CAS, other potential causes of carotid artery flow disturbance include fibromuscular dysplasia, radiation therapy, arteritis, and arterial dissection.For the purposes of this review, we will limit our discussion to atherosclerotic CAS.

Carotid atherosclerosis has important implications for both cerebrovascular health as well as that of other arterial beds. The annual incidence of stroke is ~795,000; nearly 6.6 million adult Americans have suffered a stroke, and the prevalence of transient ischemic attack (TIA) is more than 5 million.[4] Despite advances in prevention, diagnosis, and treatment, stroke remains the fourth leading cause of death in the US.[4] Approximately 87% of strokes are ischemic in nature, and 20–30% of ischemic strokes are attributable to ipsilateral carotid atherosclerosis.[4,5] Additionally, patients with carotid atherosclerosis have systemic atherosclerosis and are more likely to have clinical events in other vascular beds. Recent data found the composite risk of myocardial infarction (MI), coronary hospitalization, and cardiovascular disease (CVD) death is up to 22% higher in individuals with asymptomatic carotid atherosclerosis ≥70%.[6]

The risk of stroke due to CAS may vary by the degree of stenosis. In early studies from the 1980s, the annual risk of ipsilateral stroke in the setting of CAS ≥50% was up to 3%, and this risk increased to 5.5% with stenoses >75%.[2,7] In subsequent decades, however, the reported stroke risk has been significantly lower, and outcomes in randomized clinical trials have muted the impact of stenosis severity. These differences have been attributed both to the changing prevalence of CVD risk factors as well as the widespread use of drugs for primary and secondary prevention of CVD events. More contemporary studies have found an annual stroke risk of 0.34% and an annual TIA risk of 1.78% for patients with ≥50% CAS on medical therapy to optimize CVD risk factors.[2]

Given the prevalence of CAS and its impact on morbidity and mortality, clinicians will frequently need to make management recommendations to patients. Although routine screening for CAS is not recommended for asymptomatic patients by the US Preventative Services Task Force, many patients nevertheless undergo screening as part of bundled CVD risk assessments or following the auscultation of a carotid bruit. Other symptoms that should prompt carotid imaging as part of the clinical workup include dysarthria, weakness, and ataxia. Duplex ultrasonography is the most common imaging modality used to screen for CAS (Fig 1). Of the available imaging modalities, it is the most cost-effective and least invasive.[8] A stenotic lesion is typically defined as >50% narrowing of the ICA lumen, but the ultrasound can also detect plaque in the absence of stenosis, atherosclerosis in other extracranial arteries, and waveform abnormalities indicative of distal disease. Although less commonly used for screening purposes, CAS can also be detected with computed tomography, magnetic resonance, and invasive angiography.

Revascularization for asymptomatic CAS

For decades, investigators have examined the benefits of carotid endarterectomy (CEA) in reducing the risk of ipsilateral stroke in patients with CAS. In individuals who suffer a TIA or stroke due to CAS, there is considerably less debate regarding CEA. Accordingly, the 2014 American Heart Association/American Stroke Association guidelines make the following Class I recommendation: "For patients with a TIA or ischemic stroke within the past 6 months and ipsilateral severe (70–99%) carotid artery stenosis as documented by noninvasive imaging, CEA is recommended if the perioperative morbidity and mortality risk is estimated to be <6%."[9] However, the appropriate management of asymptomatic CAS remains controversial.

Several randomized controlled trials have examined the role of CEA for primary stroke prevention in asymptomatic CAS. The Veterans Affairs (VA) Cooperative Study Group trial, published in 1993, randomized 444 asymptomatic men with ≥50% CAS to either aspirin or aspirin plus CEA.[10] After an average follow up of ~50 months, patients in the CEA group experienced a 14.6% risk reduction in a composite outcome of ipsilateral stroke, TIA, and transient monocular blindness. The incidence of stroke alone decreased from 9.4% to 4.7% with surgical intervention. Similarly, the Asymptomatic Carotid Artery Stenosis (ACAS) trial examined 1662 patients with asymptomatic CAS ≥60%.[11] Participants were randomized to either aspirin 325 mg daily in addition to CVD risk modification or medical therapy along with CEA. Based on a

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